

AMENDMENTS

Listing of Claims

The following listing of claims replaces all previous listings or versions thereof:

1. (Currently amended) A bispecific antibody comprising ~~two~~three antibody variable domains on a single polypeptide chain, wherein:

a first portion of the bispecific antibody is capable of recruiting the activity of a human immune effector cell by specifically binding to an effector antigen located on the human immune effector cell, said first portion consisting of one antibody variable domain; and

a second portion of the bispecific antibody is capable of specifically binding to a target antigen other than the effector antigen, said target antigen being located on a target cell other than said human immune effector cell, and said second portion comprising ~~an~~two antibody variable ~~domain~~domains.

2. (Canceled)

3. (Original) The bispecific antibody of claim 1, wherein the first and second portions are derived from the same species.

4. (Original) The bispecific antibody of claim 1, wherein the first and second portions are derived from the different species.

5. (Original) The bispecific antibody of claim 1, wherein first and/or second portion are/is independently derived from a species of primate, rodent, tylopoda or cartilaginous fish.

6. (Original) The bispecific antibody of claim 5, wherein the primate-derived first and/or second portion are/is derived from man.

7. (Original) The bispecific antibody of claim 5, wherein the rodent-derived first and/or second portion are/is derived from mouse or rat.
8. (Original) The bispecific antibody of claim 7, wherein the mouse- or rat-derived first and/or second portion are/is a variable domain from the heavy chain (VH) derived from mouse or rat.
9. (Original) The bispecific antibody of claim 5, wherein the tylopoda-derived first and/or second portion are/is derived from camel, llama or dromedary.
10. (Original) The bispecific antibody of claim 9, wherein the camel-, llama- or dromedary-derived first and/or second portion is a VHH domain.
11. (Original) The bispecific antibody of claim 1, wherein the bispecific antibody has undergone an alteration to render it less immunogenic when administered to humans.
12. (Original) The bispecific antibody of claim 11, wherein the alteration comprises one or more technique selected from the group consisting of chimerization, humanization, CDR-grafting, deimmunization, and mutation of framework amino acids to correspond to the closest human germline sequence (germlining).
13. (Original) The bispecific antibody of claim 1, wherein the human effector cell is a member of the human lymphoid lineage.
14. (Original) The bispecific antibody of claim 13, wherein the effector cell is capable of exerting a cytotoxic or an apoptotic effect on a target cell.
15. (Original) The bispecific antibody of any of claim 13, wherein the effector antigen is chosen from one or more of the human CD3 antigen, the human CD16 antigen, the human NKG2D antigen, the human CD2 antigen, the human CD28 antigen and the human CD25 antigen.

16. (Original) The bispecific antibody of claim 15, wherein the effector antigen is the human CD3 antigen.
17. (Withdrawn) The bispecific antibody of claim 1, wherein the human effector cell is a member of the human myeloid lineage.
18. (Withdrawn) The bispecific antibody of claim 17, wherein the human effector cell is capable of exerting a cytotoxic or an apoptotic effect on a target cell.
19. (Withdrawn) The bispecific antibody of claim 17, wherein the human effector antigen is chosen from one or more of the human CD64 antigen or the human CD89 antigen.
20. (Original) The bispecific antibody of claim 1, wherein the target antigen is selected from EpCAM, CCR5, CD19, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neopeptide, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellierian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen; TAG-72), FAP (fibroblast activation antigen), endosialin, EGFRvIII, LG, SAS and CD63, and wherein all said antigens are human antigens.
21. (Original) The bispecific antibody of any claim 1, wherein the target antigen is a cancer-related antigen.
22. (Withdrawn) The bispecific antibody of claim 21, wherein the target antigen is the human CD19 antigen and the effector antigen is the human CD3 antigen.

23. (Original) The bispecific antibody of claim 21, wherein the target antigen is the human EpCAM antigen and the effector antigen is the human CD3 antigen.

24. (Original) The bispecific antibody of claim 23, wherein the antibody has a sequence as set out in SEQ ID NO: 1

25. (Currently amended) A bispecific antibody comprising ~~two~~three antibody variable domains on a single polypeptide chain, wherein:

a first portion of the bispecific antibody is capable of recruiting the activity of a human immune effector cell by specifically binding to an effector antigen located on the human immune effector cell, said first portion comprising ~~antwo~~ antibody variable ~~domain~~domains; and

a second portion of the bispecific antibody is capable of specifically binding to a target antigen other than the effector antigen, said target antigen being located on a target cell other than said human immune effector cell, and said second portion consisting of one antibody variable domain.

26. (Canceled)

27. (Original) The bispecific antibody of claim 25, wherein the first and second portions are derived from the same species.

28. (Currently amended) The bispecific antibody of claim 25, wherein the first and second portions are derived from ~~the same~~different species.

29. (Original) The bispecific antibody of claim 25, wherein first and/or second portion are/is independently derived from a species of primate, rodent, tylopoda or cartilaginous fish.

30. (Original) The bispecific antibody of claim 29, wherein the primate-derived first and/or second portion are/is derived from man.

31. (Original) The bispecific antibody of claim 29, wherein the rodent-derived first and/or second portion are/is derived from mouse or rat.
32. (Original) The bispecific antibody of claim 31, wherein the mouse- or rat-derived first and/or second portion are/is a variable domain from the heavy chain (VH) derived from mouse or rat.
33. (Original) The bispecific antibody of claim 29, wherein the tylopoda-derived first and/or second portion are/is derived from camel, llama or dromedary.
34. (Original) The bispecific antibody of claim 33, wherein the camel-, llama- or dromedary-derived first and/or second portion is a VHH domain.
35. (Original) The bispecific antibody of claim 25, wherein the bispecific antibody has undergone an alteration to render it less immunogenic when administered to humans.
36. (Original) The bispecific antibody of claim 35, wherein the alteration comprises one or more technique selected from the group consisting of chimerization, humanization, CDR-grafting, deimmunization, and mutation of framework amino acids to correspond to the closest human germline sequence (germlining).
37. (Original) The bispecific antibody of claim 25, wherein the human effector cell is a member of the human lymphoid lineage.
38. (Original) The bispecific antibody of claim 37, wherein the effector cell is capable of exerting a cytotoxic or an apoptotic effect on a target cell.
39. (Original) The bispecific antibody of claim 37, wherein the effector antigen is chosen from one or more of the human CD3 antigen, the human CD16 antigen, the human NKG2D antigen, the human CD2 antigen, the human CD28 antigen and the human CD25 antigen.

40. (Original) The bispecific antibody of claim 39, wherein the effector antigen is the human CD3 antigen.
41. (Withdrawn) The bispecific antibody of any of claim 25, wherein the human effector cell is a member of the human myeloid lineage.
42. (Withdrawn) The bispecific antibody of claim 41, wherein the effector cell is capable of exerting a cytotoxic or an apoptotic effect on a target cell.
43. (Withdrawn) The bispecific antibody of claim 41, wherein the effector antigen is chosen from one or more of the human CD64 antigen or the human CD89 antigen.
44. (Original) The bispecific antibody of claim 25, wherein the target antigen is selected from EpCAM, CCR5, CD19, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neoepitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellierian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen; TAG-72), FAP (fibroblast activation antigen), endosialin, EGFRvIII, LG, SAS and CD63, and wherein all said antigens are human antigens.
45. (Original) The bispecific antibody of any claim 25, wherein the target antigen is a cancer-related antigen.
46. (Withdrawn) The bispecific antibody of claim 45, wherein the target antigen is the human CD19 antigen and the effector antigen is the human CD3 antigen.

47. (Original) The bispecific antibody of claim 45, wherein the target antigen is the human EpCAM antigen and the effector antigen is the human CD3 antigen.
48. (Original) The bispecific antibody of claim 47, wherein the antibody has a sequence as set out in SEQ ID NO: 1.
49. (Withdrawn) A nucleotide sequence encoding SEQ ID NO: 1 or a nucleotide sequence exhibiting at least 70% homology therewith, wherein homology is determined by comparing a nucleotide sequence encoding SEQ ID NO: 1 with a nucleotide sequence in question by sequence alignment, and wherein a nucleotide in the sequence in question is considered homologous if it is either identical to the corresponding nucleotide in the nucleotide sequence encoding SEQ ID NO: 1 or if deviation in a nucleotide in the sequence in question from the corresponding nucleotide in the nucleotide sequence encoding SEQ ID NO: 1 results in a nucleotide triplet which, when translated, results in an amino acid which is either identical with or creates a conservative substitution of the amino acid at the corresponding position in the amino acid sequence of SEQ ID NO: 1.
50. (Withdrawn) A method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, an allergic reaction, a parasitic reaction, a graft-versus-host disease or a host-versus-graft disease in a subject in the need thereof, said method comprising the step of administration of an effective amount of a bispecific antibody of claim.
51. (Withdrawn) The method of claim 50, wherein said subject is a human.
52. (Withdrawn) The method of claim 50, further comprising the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells.
53. (Withdrawn) The method of claim 52, wherein said proteinaceous compound is administered simultaneously or non-simultaneously with a bispecific antibody of any of claim 1.

54. (Withdrawn) A method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, an allergic reaction, a parasitic reaction, a graft-versus-host disease or a host-versus-graft disease in a subject in the need thereof, said method comprising the step of administration of an effective amount of a bispecific antibody of claim 25.

55. (Withdrawn) A method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, an allergic reaction, a parasitic reaction, a graft-versus-host disease or a host-versus-graft disease in a subject in the need thereof, said method comprising the step of administration of an effective amount of a bispecific antibody of a nucleotide sequence of claim 49.

56. (Currently amended) A kit comprising a bispecific antibody of ~~any~~ of claim 1.

57. (Currently amended) A kit comprising a bispecific antibody of ~~any~~ of claim 25.